REMARKS

The Office Action dated May 21, 2008 has been carefully reviewed and the foregoing remarks are made in response thereto. In view of the following remarks and amendments to the claims, Applicants respectfully request reconsideration of this application and the timely allowance of the pending claims.

I. Summary of the Office Action.

1. Claims 1, 3, 5-17 and 19-21 are pending. Claims 5-17 are withdrawn from consideration.

2. The Examiner has rejected claims 1, 3 and 19-21 under 35 U.S.C. § 103 as allegedly obvious over Ellsworth *et al.* Society for Neuroscience Abstracts. 2001; 27(2): 2026 (abstract), in view of U.S. Patent Application Publication No. 2001/0039261 to Finkelstein.

3. No claims are allowed.

II. Response to the Office Action.

By this amendment, claims 1 and 3 are amended. Claims 18 and 19 are cancelled. Support for the amendment to claim 1 is found in the specification at paragraphs 0013, 0015, 0017 and Example 1 (as discussed further below). Support to the amendment of claim 3 is found in the specification at least at paragraphs 0001, 0007, and 0021. No new matter is added by these amendments.

1. Claim rejections under 35 U.S.C. § 103—Obviousness

The Examiner has rejected claims 1, 3, and 19-21 under 35 U.S.C. § 103, as allegedly obvious over Ellsworth *et al.* in view of Finkelstein. According to the Examiner, Ellsworth *et al.* teach intravenous infusion of FGF-18 for the improvement of memory in rats with impaired cognitive performance following cerebral artery occlusion, thereby enhancing memory, attentive cognition, or learning as recited in the pending claims. Although the Examiner concedes that Ellsworth *et al.* do not teach administration to humans, the Examiner contends that Finkelstein teaches a method of administering an FGF protein to a human to treat a CNS injury, resulting in enhanced cognitive performance. Finkelstein does not disclose that the FGF protein can be FGF-18, but the Examiner alleges that on of ordinary skill in the art would have been motivated by the combined teachings of Ellsworth *et al.* and

Finkelstein to use FGF-18 to enhance memory, attentive cognition, and/or learning in humans.

Applicants respectfully request withdrawal of this rejection. As noted above, the abstract by Ellsworth *et al.* disclose that FGF-18 improves reference and working memory in rats following cerebral ischemia cause by stroke. Ellsworth *et al.* do not teach that FGF-18 can enhance memory, attentive cognition or learning in an animal or human subject who has not been subjected to/afflicted with cerebral ischemia, *i.e.* with no impairment. Finkelstein does not remedy this deficiency. The disclosure in Finkelstein, too, is limited to using bFGF to treat neuronal damage resulting from cerebral ischemia, *i.e.*, stroke. Further, Finkelstein does not even mention enhancing memory, attentive cognition, or learning—Finkelstein teaches only that use of bFGF improves post-ischemic **sensorimotor** deficits. This is evidenced by the fact that none of the functional tests disclosed by Finkelstein on page 6, paragraphs 0063-0067 are designed to evaluate memory, cognition, or learning, but are designed to measure sensory or motor defects. Accordingly, one of ordinary skill in the art seeking to enhance memory, attentive cognition, and/or learning would not have looked to Finkelstein for guidance.

The combination of Ellsworth *et al.* and Finkelstein cannot render claim 1 obvious because the combination of references do not teach or suggest a method of using FGF-18 to enhance memory, attentive cognition, and learning in humans not having deficits in the foregoing as recited by claim 1 (as amended). Both Ellsworth *et al.* and Finkelstein are wholly concerned with treating post-ischemic neuronal injury using FGFs, the difference being that Ellsworth *et al.* uses FGF-18 to improve reference and working memory and motor activity, and Finkelstein uses bFGF to improve sensorimotor deficits. At most, a combination of these to references teaches that use of FGFs to treat post-ischemic deficits is a good bet.

Applicants recognize that any negative limitation or exclusionary proviso must have basis in the original disclosure. If alternative elements are positively recited in the specification, they may be explicitly excluded in the claims. *See In re Johnson*, 558 F.2d 1008, 1019 (CCPA 1977) ("[the] specification, having described the whole, necessarily described the part remaining."). *See also Ex parte Grasselli*, 231 USPQ 393 (Bd. App. 1983), aff'd mem., 738 F.2d 453 (Fed. Cir. 1984). *See also* MPEP 2173.05(i). However, it is clear from the specification that the present invention positively recites the alternative

embodiments of enhancing memory, attentive cognition, and learning in humans *without* deficits in memory, attentive cognition, and learning and *with* deficits. See, for example, the following statements in the specification:

> Applicants....have discovered that administration of exogenous FGF-18 significantly enhances the performance of animals in the Morris water maze test. <u>In a first aspect</u>, the invention provides a method of enhancing learning and memory consolidation in an animal, which comprises administering an effective amount of FGF-18.

See paragraph 0013 (emphasis added).

> The invention <u>also</u> provides for the use of FGF-18 to facilitate learning and memory, and to treat subjects suffering from impaired learning and/or memory functions.

See paragraph 0015 (emphasis added).

> The invention provides a method of enhancing memory, attentive cognition or learning comprising the administration of a composition, wherein the composition comprises an effective amount of FGF-18 and a pharmaceutically acceptable carrier, to a subject in need thereof. <u>In a preferred embodiment</u>, the subject suffers from a condition selected from the group consisting of: impaired cognitive performance, learning deficit, cognition deficit, attention deficit, epilepsy, schizophrenia, Alzheimer's disease, and amnesiac syndromes.

See paragraph 0017 (emphasis added).

> As used herein, "enhancement in memory, attentive cognition or learning" refers to an improvement in memory, attentive cognition or learning as compared to a control subject or the subject prior to treatment.

See paragraph 0064.

Example 1 provides further evidence that an embodiment of invention is directed to enhancing memory, attentive cognition and learning in the absence of deficits in the foregoing.

In view of the above, Applicants respectfully request withdrawal of the rejection of claims 1, 20 and 21. Claim 19 has been cancelled by this amendment, obviating the rejection over this claim.

Nor do the combination of references render obvious claim 3. Claim 3, as currently amended, is directed to a method of treating impaired cognitive performance in a human using FGF-18, where the impaired cognitive performance is associated with impaired function of the hippocampus. Support for the amendment of claim 9 is found in the specification at *e.g.*, paragraphs 0001, 0007 and 0021. Neither Ellsworth *et al.* nor Finkelstein disclose using any FGF to ameliorate impaired cognitive performance associated with impaired function of the hippocampus.

Applicants further submit that neuronal damage to the hippocampus is not necessarily implicated in models of cerebral ischemia disclosed in Ellsworth *et al.* and Finkelstein. Both Ellsworth *et al.* and Finkelstein disclose induction of cerebral ischemia by occlusion of the <u>middle cerebral artery</u>. *See* line 7 of Ellsworth *et al.* and paragraph 0055 of Finkelstein. This model is commonly used when damage to the cortex, particularly the frontal and parietal areas of the cortex, is sought. *See* paragraph 0075 of Finkelstein. *See also* Exh. 1 (abstract of Menzie *et al.*, internet printout from **www.strokecenter.org**). Typical impairment resulting from middle cerebral artery occlusion (MCAo) includes weakness and sensory loss in the extremities and lower face, aphasia (impaired speech), hemineglect (lack of awareness of items to one side of space), lateral gaze weakness, and visual loss. *See* internet printout from **www.strokecenter.org** at Exh. 2.

In contrast, to induce ischemic neuronal damage to the hippocampus, occlusion of the <u>carotid</u> arteries is performed. *See* abstracts of Bond *et al.* and Tagami *et al.* at Exh. 3. Moreover, even carotid artery occlusion will not *necessarily* impair the hippocampus in every instance under every circumstance. *See* abstract of Tagami *et al.* at Exh. 3, which states that apoptosis of hippocampal neurons in a carotid artery occlusion model of ischemia did not induce apoptosis in hippocampal neurons in Wistar Kyoto rats.

It is also submitted that the areas of the cortex that are infarcted (damaged) by MCAo, adversely affect both reference and working memory. The prefrontal cortex is well-known to be implicated in working memory (short term). *See* abstracts of Misoguchi, and printout from http://thebrain.mcgill.ca at Exh. 4. Other areas of the brain, including the parietal cortex, perhinal cortex, and anterior cingulate xortexare involved in reference memory. *See* abstracts of Soblosky *et al.*, Wig *et al.*, and Maviel *et al.* at Exh. 5. As such,

damage to areas of the cortex, such as those damaged in the ischemic models taught by the prior art, can adversely impact both working reference memory.

The hippocampus is not within the cortex. Accordingly, Applicants contend that because neither Ellsworth *et al.* nor Finkelstein teach or suggest that the deficits resulting from cerebral ischemia are caused by impairment of the hippocampus, and because the model used by both is not a model used to evaluate injury to the hippocampus, the references alone or in combination do not render claims 3, 20 and 21 obvious.

In view of the foregoing, withdrawal of this rejection is respectfully requested.

III. Other Comments

The Examiner has previously rejected a claim containing a limitation to increasing FGF-18 in the hippocampus. The Examiner alleged that because it is well known in the art that the hippocampus is involved in memory consolidation and working memory, the use of FGF-18 as described in Ellsworth *et al.* inherently anticipated the claim. See Office Action dated August 17, 2007. This rejection was overcome by removing the limitation. However, Applicants address this here in view of the current amendment to Claim 3, which recites that a method of treating cognitive impairment associated with an impairment to the hippocampus.

"In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic <u>necessarily</u> flows from the teachings of the applied prior art." MPEP § 2112 IV (citing *Ex parte Levy,* 17 U.S.P.Q. 2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original)). The fact that a certain result or characteristic <u>may</u> occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. MPEP § 2112 IV (citing *In re Rijckaert,* 9 F.3d 1531, 1534 (Fed. Cir. 1993) (reversed rejection because inherency was based on what would result due to optimization of conditions, not what was necessarily present in the prior art)).

For the reasons provided in Section II, above, Applicants contend that the ischemic stroke model used by Ellsworth *et al.* (and Finkelstein), in which the middle cerebral artery is occluded (MCAo), would not *necessarily* impair the hippocampus. Applicants have established i) that the MCAo primarily affects the frontal and parietal cortex region of the brain, ii) that different arteries are occluded when damage to the hippocampus is

sought, and **iii)** that the impairment in working and reference memory observed by Ellsworth *et al.* using the MCAo model is consistent with damage to the frontal and parietal cortex regions that are infarcted in that model and does not necessarily result from damage to the hippocampus.

Thus, it is clear that Ellsworth *et al.* do not inherently disclose administration of FGF-18 to treat impaired cognitive performance in a human subject, where the impaired cognitive performance is associated with impaired function of the hippocampus.

IV. Conclusion.

Applicants believe that the above-referenced application is in condition for allowance. Reconsideration and withdrawal of the outstanding rejections and early notice of allowance to that effect is respectfully requested.

> **EXCEPT** for issue fees payable under 37 C.F.R. § 1.18, the Director is hereby authorized by this paper to charge any additional fees during the entire pendency of this application, including fees due under 37 C.F.R. §§ 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account No. 13-3250, reference No. 17357.01202US. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 C.F.R. § 1.136(a)(3).

If the Examiner finds that a telephone conference would further prosecution of this application, the Examiner is invited to contact the undersigned at 202-835-7553.

Respectfully submitted,

MILBANK, TWEED, HADLEY & MCCLOY LLP

Dated: August 21, 2008

51,401 for Stephane Amoroso

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EXHIBIT 1

Note: Performing your original search, ***occlusion of the middle cerebral artery***, in PubMed will retrieve 8935 citations.

1: Neurosurgery. 1992 Jul;31(1):100-6; discussion 106-7.

Comment in:
Neurosurgery. 1993 Mar;32(3):479.

Middle cerebral artery occlusion in rats: a neurological and pathological evaluation of a reproducible model.

Menzies SA, Hoff JT, Betz AL.

Department of Surgery, University of Michigan, Ann Arbor.

Middle cerebral artery occlusion (MCAO) in rats produces an infarct of varying size. We examined three factors that may influence this variability: animal weight, vascular anatomy, and extent of occlusion in rats undergoing MCAO. We also developed a four-point neurological evaluation scale and validated its usefulness by comparing it with a four-grade pathological determination of the size of the infarct. Of 82 animals subjected to a standard MCAO, 34 developed small cortical infarcts (pathological grades I-II; infarct size less than 25 mm2, 6-17% of the ipsilateral cortex surface area), and 48 large infarcts (pathological grades III-IV, infarct size greater than 25 mm2, 20-56% of surface area). We were able to predict the size of infarction from the neurological evaluation in 83% of the animals, and this accuracy reached 91% when grades I and II and III and IV were considered together (P less than 0.001). In 41 animals subjected to a more extensive vascular occlusion, 89% exhibited large infarcts. Four vascular patterns were identified but none played a significant role in the incidence or size of the cortical stroke. However, rats weighing less than 300 g showed a smaller lesion size than did rats greater than 300 g. Our proposed new MCAO technique appears useful in reproducing large-sized infarcts of the frontoparietal cortex.

PMID: 1641086 [PubMed - indexed for MEDLINE]

Related Articles

- Rat middle cerebral artery occlusion: evaluation of the model and development of a neurologic examination. [Stroke. 1986]
- Middle cerebral artery occlusion in the mouse by intraluminal suture coated with poly-L-lysine: neurological and histological validation. [Brain Res. 1999]
- Middle cerebral artery occlusion in the rat by intraluminal suture. Neurological and pathological evaluation of an improved model. [Stroke. 1996]
- Mild focal cerebral ischemia in the rat. The effect of local temperature on infarct size. [Neurol Res. 2002]
- Focal brain ischemia in the rat: methods for reproducible neocortical infarction using tandem occlusion of the distal middle cerebral and ipsilateral common carotid arteries. [J Cereb Blood Flow Metab. 1988]

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Brain Anatomy

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MRI Compared to CT

Stroke Facts

Epidemiology of Stroke

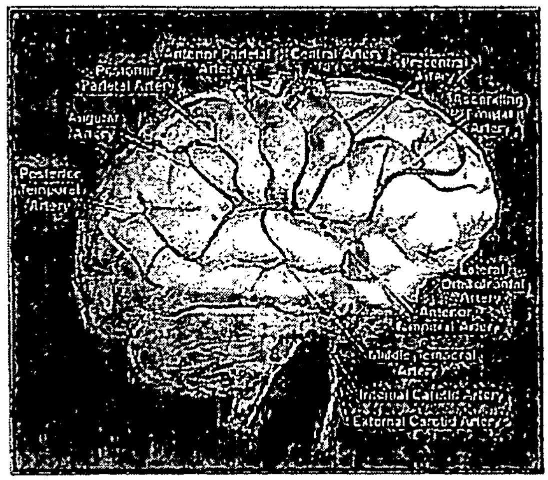
Stroke Risk Factors

Types of Stroke

Blood Vessels of the Brain

Middle Cerebral Artery

The middle cerebral artery is the largest branch of the internal carotid. The artery supplies a portion of the frontal lobe and the lateral surface of the temporal and parietal lobes, including the primary motor and sensory areas of the face, throat, hand and arm and in the dominant hemisphere, the areas for speech. The middle cerebral artery is the artery most often occluded in stroke.



Click on image to enlarge.

◀ Back Contents Next ▶

From: Acute Ischemic Stroke: New Concepts of Care

Click here for information about this CD.

EXHIBIT 2

Stroke Diagnosis

In this Section:
Diagnostic Tests | Imaging | Image Library | Stroke Scales | Stroke Syndromes
Syndromes Arranged by: Vascular Territory | Eponym | Syndrome Name

Stroke Syndromes

Middle cerebral artery - complete

Eponym:

Anatomy:

Vascular: Middle cerebral artery: Proximal occlusion at MCA stem

Signs & Symptoms:

*Side:	Manifestation:	Comments:
C	Weakness - upper and lower extremity	Somatic motor area for face, arm > leg
C	Weakness - face - lower half	
C	Hemisensory loss - upper and lower extremity	
C	Sensory loss - face - all modalities	
N	Aphasia - receptive	Dominant hemisphere (Wenicke's area)
N	Aphasia - expressive	Dominant hemisphere (Broca's area)
C	Hemineglect	Non-dominant hemisphere
C	Lateral gaze weakness	
I	Gaze preference	
C	Visual loss - homonymous hemianopia	

*Side: Ipsilateral, Contralateral, Both, Neither

Updated: 7/20/1999

EXHIBIT 3

Neuroprotective effects of a systemically active Group II metabotropic glutamate receptor agonist LY354740 in a gerbil model of global ischaemia.

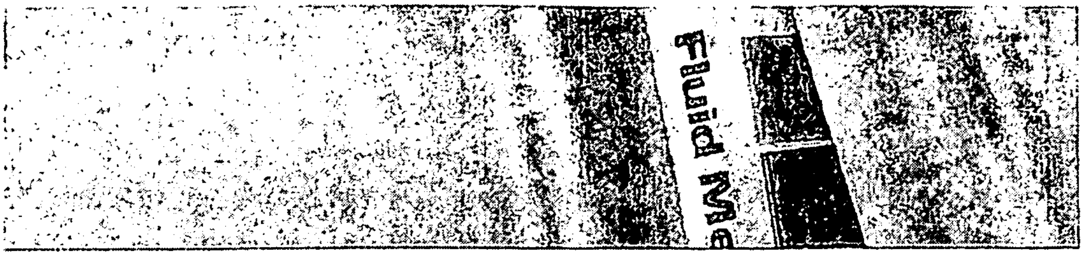
Neuropharmacology and Neurotoxicology

Neuroreport. 9(6):1191-1193, April 20, 1998.

Bond, Ann 1,3; O'Neill, Michael J. 1; Hicks, Caroline A. 1; Monn, James A. 2; Lodge, David 1

Abstract:

THE neuroprotective effects of a novel Group II metabotropic glutamate receptor (mGluR) agonist, LY354740, have been evaluated in a gerbil model of global ischaemia. When administered at 50 mg/kg, i.p., 30 min and 6 h after a 3 min period of bilateral carotid artery occlusion (BCAO), the compound reduced the damage to CA1 hippocampal neurones to a significant level. However, when the ischaemic insult was made more severe, by increasing the period of occlusion to 4 and 5 min, the neuroprotective effects of LY354740 were reduced. From these findings, it would appear that Group II mGluRs may play a role in ischaemic damage in the gerbil hippocampus and that agonists at these receptors are potential neuroprotective agents.



Titre du document / Document title

Vitamin E prevents apoptosis in hippocampal neurons caused by cerebral ischemia and reperfusion in stroke-prone spontaneously hypertensive rats

Auteur(s) / Author(s)

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Résumé / Abstract

Cerebral ischemia followed by oxygen reperfusion induced apoptosis in hippocampal neurons in stroke-prone spontaneously hypertensive rats (SHRSP) but not in Wistar Kyoto rats. Oxygen radicals were involved in reoxygenation injury after hypoxia in hippocampal slices. Vitamin E inhibited the reoxygenation injury in cultured cortical neurons. In addition, the temporal cortices in Alzheimer's disease have increased sensitivity to oxygen radicals, and Vitamin E slowed the progression of the disease. Thus we fed Wistar Kyoto and SHRSP rats either a normal diet or a high Vitamin E diet for 3 weeks. We measured Vitamin E concentrations of plasma and brain by applying the HPLC method. Vitamin E increased its concentration in plasma, cerebral cortex, and hippocampus ($p < 0.01$) during a 3-week pretreatment. In addition, we clipped both common carotid arteries in these rats for 30 minutes. After the blocking, the rats were reperfused for 6 and 9 days, respectively, and then killed. We cut the brains coronally, removed the hippocampal CA1 regions, and examined the neurons using an electron microscope. SHRSP rats with normal cerebral circulation had 30.4 ± 8.0 apoptotic neurons per 1000 neurons. Cerebral ischemia followed by 6 and 9 days of reperfusion, respectively, increased apoptotic neurons in SHRSP rats fed a normal diet (6 days: $542.5 \pm 154.$ per 1000 neurons; 9 days: 657.5 ± 110.2 per 1000 neurons). In contrast, apoptotic neurons in SHRSP rats fed a high Vitamin E diet were significantly ($p < 0.01$) small in number (6 days: 41.3 ± 27.5 per 1000 neurons; 9 days: 35.5 ± 19.7 per 1000 neurons) even though the rats were treated in the same way. These data demonstrate that oxygen radical generation occurs after reperfusion and that free radicals heavily damage the neurons in SHRSP rats. Vitamin E reacts with the radicals and prevents neuronal apoptosis caused by cerebral ischemia and reperfusion. Therefore, Vitamin E seems to be an important agent in lowering radical damage to hippocampal neurons.

Revue / Journal Title

Laboratory investigation ISSN 0023-6837 CODEN LAINAW

Source / Source

1999, vol. 79, n°5, pp. 609-615 (25 ref.)

Langue / Language

Anglais

Editeur / Publisher

Nature Publishing, New York, NY, ETATS-UNIS (1952) (Revue)

Mots-clés anglais / English Keywords

Ischemia ; Brain (vertebrata) ; Reperfusion ; Pathophysiology ; Apoptosis ; E-Vitamins ; Supplementation ; Cerebral cortex ; Hippocampus ; Chelating agent ; Free radical ; Oxygen ; Experimental study ; Animal ; Rat ;

EXHIBIT 4

Brain Research
Volume 915, Issue 1, 5 October 2001, Pages 108-111

doi:10.1016/S0006-8993(01)02834-7

Short communication

Effect of chronic stress on cholinergic transmission in rat hippocampus

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Accepted 12 July 2001. Available online 17 August 2001.

Abstract

We previously demonstrated that chronic stress impaired prefrontal cortex-sensitive working memory, but not reference memory. Since the hippocampal

cholinergic system is also involved in these memories, we examined the effects of chronic stress on cholinergic transmission in the rat hippocampus. A microdialysis study revealed that the stress did not affect the basal acetylcholine release, but enhanced the KCl-evoked response. These results suggest that cholinergic transmission in the chronically stressed hippocampus does not contribute to working memory impairment, but it may be involved in maintenance of reference memory.

Author Keywords: Chronic stress; Acetylcholine; Choline; Microdialysis; Hippocampus; Rat

Article Outline

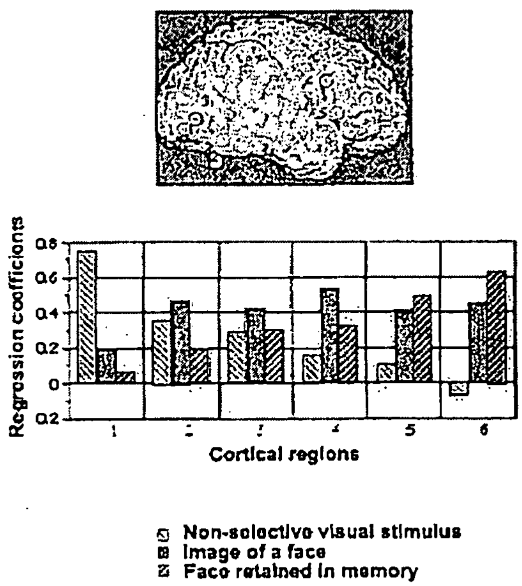
Brain Research
Volume 915, Issue 1, 5 October 2001, Pages 108-111

SHORT-TERM MEMORY

A large body of evidence indicates that the dorsolateral prefrontal cortex plays an important role in cer forms of memory work, in particular those that involve alternating between two memory tasks and expl various possibilities before making a choice.

It seems fairly certain that this area of the brain holds information required for reasoning processes th in progress. But its precise role remains the subject of much debate. Does this prefrontal area basicall coordinate the activities of slave sub-systems, as in Baddeley's model of the phonological loop and th visual/spatial sketchpad? Or does it actually itself serve as a temporary storage area for certain types information, as Goldman-Rakic's research tends to indicate? Might the level of abstraction of the task i the deciding factor, or might the size of the workload determine whether this area comes into play?

As all these unanswered questions suggest, the anatomical substrate of working memory is far from b understood in detail. Moreover, the phenomenon of working memory is made all the more complex by fact that it takes place over time.



Source: NIMH Laboratory of Brain and Cognition. Published in *Nature*, Vol. 386, April 1997, p. 610.

For example, the experimental results illustrated here show how various areas o subjects' brains alter their activity levels a subjects are presented with various visual stimuli. When the subjects are shown a bl image, the activity level (represented by tl blue bars in the graph) becomes highest i area 1, the visual part of the brain. When subjects are shown an image of a face, bı activity (black bars) becomes highest in th associative and frontal regions (4, 5, and t Lastly, when the subjects are retaining an image of a face in their working memory, t activity (red bars) is highest in the frontal regions, while the visual areas are scarce stimulated at all.

It has also been observed that distinct processes appear to be involved in the st and recall of items memorized with the phonological loop and the visual/spatial sketchpad.

One thing is certain: the prefrontal cortex plays a fundamental role in working memory. It enables peo keep information available that they need for their current reasoning processes. For this purpose, the prefrontal cortex must cooperate with other parts of the cortex from which it extracts information for bri periods. For this information to eventually pass into longer-term memory, the limbic system probably h be brought into play.

EXHIBIT 5

Titre du document / Document title
Reference memory and allocentric spatial localization deficits after unilateral cortical brain injury in the rat

Auteur(s) / Author(s)
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[2] Department of Anatomy, Louisiana State University Medical Center, New Orleans, LA, ETATS-UNIS

Résumé / Abstract
Traumatic brain injury (TBI) produces learning and memory impairments in humans. This study investigated the effects of TBI on memory and spatial localization strategies in rats. Prior to TBI, separate groups of rats were trained in an 8-arm radial maze with either all 8 arms baited (Expt. 1) or only 4 of the 8 arms baited (Expt. 2). TBI was produced by a controlled pneumatic impactor striking the entire right sensorimotor cortex of the anesthetized rat. Rats used in Expt. 1 were selected because they did not use a stereotypic response strategy (going to adjacent arms) in performing the maze before injury. After TBI the rats were not different from control rats in the number of working memory (WM) errors made. They did, however, display a distinct propensity to go to adjacent arms, i.e., exhibit stereotypic behavior, with a right-handed (ipsiversive) bias ($P<0.005$). After TBI, rats which were trained with only 4 of 8 arms baited committed more reference memory (RM) errors than control rats ($P<0.05$). They did not differ from controls on WM errors. Injured rats took longer to re-attain criteria than controls ($P<0.0001$). Injured rats also initially displayed a propensity to enter the adjacent arm sequentially before re-attaining criteria. Further analysis indicated that injured rats re-learned the maze with a right-hand bias ($P<0.0001$). The results of both experiments suggest that after TBI, rats shifted from an allocentric to an egocentric strategy to re-learn the maze. It was suggested that damage to the parietal cortex may have been responsible for both RM errors and the shift away from an allocentric strategy to an egocentric strategy. Possibly, the ipsiversive (right-hand) bias may be the result of a behaviorally or injury-induced neurochemical asymmetry within the motor system.

Revue / Journal Title
Behavioural brain research ISSN 0166-4328 CODEN BBREDI

Source / Source
1996, vol. 80, n°1-2, pp. 185-194 (51 ref.)

Langue / Language
Anglais

Editeur / Publisher
Elsevier Science, Shannon, IRLANDE (1980) (Revue)

Mots-clés anglais / English Keywords
Reference memory ; Space perception ; Cerebral cortex ; Lesion ; Perceptive learning ; Male ; Animal ; Rat ; Brain (vertebrata) ; Central nervous system ; Acquisition process ; Perception ; Rodentia ; Mammalia ; Vertebrata ;

Mots-clés français / French Keywords
Mémoire référence ; Perception espace ; Cortex cérébral ; Lésion ; Apprentissage perceptif ; Mâle ; Animal ; Rat ; Rat Sprague Dawley ; Labyrinthe radial ; Encéphale ; Système nerveux central ; Processus acquisition ; Perception ; Rodentia ; Mammalia ; Vertebrata ;

Titre du document / Document title
The effects of perirhinal cortical lesions on spatial reference memory in the rat

Auteur(s) / Author(s)
WIIG K. A. ; BILKEY D. K. ;

Affiliation(s) du ou des auteurs / Author(s) Affiliation(s)
Univ. Otago, neurosci. res. cent., dep. psychology, Dunedin, NOUVELLE-ZELANDE

Résumé / Abstract
Rats with bilateral, electrolytic lesions of the perirhinal cortex and sham operated control rats were tested in the Morris water maze, a procedure which has repeatedly been shown to be sensitive to hippocampal and limbic system dysfunction. The results of the present study demonstrate that perirhinal lesioned rats were mildly impaired on this task. The lesioned animals took significantly longer than controls to locate the hidden platform during place navigation acquisition, and had significantly larger heading errors across the entire experimental procedure. In addition, these lesioned animals made fewer platform crossings than control rats during the probe trials. These results suggest that the perirhinal cortex, like the anatomically related entorhinal cortex and hippocampus, may be involved in mnemonic processing

Revue / Journal Title
Behavioural brain research ISSN 0166-4328 CODEN BBREDI

Source / Source
1994, vol. 63, n°1, pp. 101-109 (37 ref.)

Langue / Language
Anglais

Editeur / Publisher
Elsevier Science, Shannon, IRLANDE (1980) (Revue)

Mots-clés anglais / English Keywords
Spatial memory ; Reference memory ; Perirhinal cortex ; Lesion ; Spatial orientation ; Information processing ; Male ; Animal ; Rat ; Brain (vertebrata) ; Central nervous system ; Cognition ; Rodentia ; Mammalia ; Vertebrata ;

Mots-clés français / French Keywords
Mémoire spatiale ; Mémoire référence ; Cortex périrhinal ; Lésion ; Orientation spatiale ; Traitement information ; Mâle ; Animal ; Rat ; Labyrinthe immergé Morris ; Rat Sprague Dawley ; Encéphale ; Système nerveux central ; Cognition ; Rodentia ; Mammalia ; Vertebrata ;

Mots-clés espagnols / Spanish Keywords
Memoria espacial ; Memoria referencia ; Corteza perirrinal ; Lesión ; Orientación espacial ; Procesamiento información ; Macho ; Animal ; Rata ; Encéfalo ; Sistema nervioso central ; Cognición ; Rodentia ; Mammalia ; Vertebrata ;

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Sites of Neocortical Reorganization Critical for Remote Spatial Memory

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The hippocampus is crucial for spatial memory formation, yet it does not store long-lasting memories. By combining functional brain imaging and region-specific neuronal inactivation in mice, we identified prefrontal and anterior cingulate cortex as critical for storage and retrieval of remote spatial memories. Imaging of activity-dependent genes also revealed an involvement of parietal and retrosplenial cortices during consolidation of remote memory. Long-term memory storage within some of these neocortical regions was accompanied by structural changes including synaptogenesis and laminar reorganization, concomitant with a functional disengagement of the hippocampus and posterior cingulate cortices. Thus, consolidation of spatial memory requires a time-dependent hippocampal-cortical dialogue, ultimately enabling widespread cortical networks to mediate effortful recall and use of cortically stored remote memories independently.

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